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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/960,244
Filing Date: September 21, 2001
Appellant(s): HO ET AL.

Doyle Siever
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1/25/2010 appealing from the Office action mailed 3/16/2009.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

Subsequent to filing the instant brief, Appellant's have appealed case 10/251685.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

14, 21, 25-26 & 97 are pending and stand rejected.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief other than to say that the amendment filed with the appeal brief was in clear violation of 37 CFR 41.33(b) and (c) and as such could not be entered.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS."

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner.

Claim 97 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 97 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Appellant's arguments were persuasive to overcome these two section 112 rejections.

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

5733542 Haynesworth et al 1998

Pittenger et al. Science 284: 143-147. 1999

Woodbury et al Journal of Neuroscience Research 61:364-370 2000.

Lee et al Hepatology 40: 1275-1284. 2000.

Chamberliain et al. Stem Cells 2007 25:2739-2749.

Baksh et al. J Cell Mol Med Vol 8(3) 2004: 301-316

Lodie et al. Tissue Engineering. Vol8(5) 2002. 739-751

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 14, 21, 25-26 & 97 stand finally rejected under 35 U.S.C. 102(b) as being anticipated by Haynesworth et al. (1998, U.S. Patent 5,733,542) taken in light of Pittenger et al. (1999, *Science* 284: 143-147), Woodbury et al. (2000, *Journal of Neuroscience Research* 61: 364-370), and Lee et al. (2000, *Hepatology* 40: 1275-1284).

Appellants claim an isolated population of bone marrow cells. Appellants further identify the cells by certain immunological markers and the doubling rate of the cells.

Haynesworth et al. teach a population of mesenchymal stem cells (MSCs) isolated from human adult bone marrow. Appellants do not identify their cells as stem cells but analysis of the prior art and claimed cells will show that they are the same cells and the instantly claimed properties are inherent to the cells of Haynesworth:

In Haynesworth (example 1), marrow is taken from the iliac crest as is done in Appellants' examples. A "low oxygen" culture is used (95% air/5% CO_2) to culture the marrow cells and obtain an adherent cell population (CFUs) which is a population of MSCs. Haynesworth is silent on the presence or absence of CD49c and CD90 or on the specific doubling rate of the cell population. However, as the claimed cells are isolated from the same source and in the same manner as the cells of Haynesworth, the cells must necessarily be the same.

Further, (although unclaimed) Appellants disclose in their specification that the cell population is pluripotent and has a particular neuronal therapeutic use. The bone-marrow derived mesenchymal cells of Haynesworth have same inherent quailities as evidenced by Pittenger et al. who teach that the MSCs of Haynesworth et al. can differentiate to various mesodermal cell lineages, including bone, cartilage, and adipose (Figure 2). Woodbury et al. is cited as evidence that the MSCs of Haynesworth et al. can differentiate to neurons, (page 364, column 1, paragraph 1; page 365, column 2, paragraph 2, through page 367, column 2, paragraph 3). Further evidence of the pluripotent nature of the MSCs is also shown in Lee et al. who teach that the MSCs of Haynesworth et al. can differentiate to hepatocytes, (page 1277, column 1, paragraph 3; page 1279, column 1, paragraphs 2 and 3; Figure 2).

To invalidate a patent by anticipation, a prior art reference normally needs to disclose each and every limitation of the claim. See *Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 953 F.2d 1360, 1369, 21 USPQ2d 1321, 1328 (Fed. Cir. 1991). However, a prior art reference may anticipate when the claim limitation or limitations not expressly found in that reference are nonetheless inherent in it. See *id.* and *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 630, 2 USPQ2d 1051,1053 (Fed. Cir. 1987). Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates. See *In re King*, 801 F.2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. See *Titanium Metals*, 778 F.2d at 780. Artisans of ordinary skill may not recognize the inherent

characteristics or functioning of the prior art. See *id.* at 782. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. See *id.* at 782 ("Congress has not seen fit to permit the patenting of an old [composition], known to others…, by one who has discovered its…useful properties."); *Verdegaal Bros.*, 814 F.2d at 633.

This court's decision in *Titanium Metals* illustrates these principles. See *Titanium Metals*, 778 F.2d at 775. In *Titanium Metals*, the patent applicants sought a patent for a titanium alloy containing various ranges of nickel, molybdenum, iron, and titanium. The claims also required that the alloy be "characterized by good corrosion resistance in hot brine environments." *Titanium Metals*, 778 F.2d at 776. A prior art reference disclosed a titanium alloy falling within the claimed ranges, but did not disclose any corrosion-resistant properties. This court affirmed a decision of the PTO Board of Appeals finding the claimed invention unpatentable as anticipated. This court concluded that the claimed alloy was not novel, noting, "it is immaterial, on the issue of their novelty, what inherent properties the alloys have or whether these applicants discovered certain inherent properties." *Id.* at 782. This same reasoning holds true when it is not a property, but an ingredient, which is inherently contained in the prior art. The public remains free to make, use, or sell prior art compositions or processes, regardless of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate. The doctrine of anticipation by inherency,

among other doctrines, enforces that basic principle." See *Atlas Powder Co. v. IRECO Inc.*, 51 USPQ2d 1943 (Fed. Cir. 1999).

Thus, a reference may be anticipatory if it discloses every limitation of the claimed invention either explicitly or inherently. A reference includes an inherent characteristic if that characteristic is the natural result flowing from the reference's explicitly explicated limitations. *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

While the prior art does not clearly disclose all of Appellants' claimed limitations, it would appear that the cells claimed are a population of MSCs as disclosed by Haynesworth. M.P.E.P. § 2112 reads, "The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable." Something that is old does not become patentable upon the discovery of a new property, use, or application. Even if Appellants had identified properties of the MSCs of Haynesworth et al. that Haynesworth et al. did not or could not test for, such an identification would not render the MSCs of Haynesworth et al. patentable. As such, the claimed expressions and doubling rates are merely inherent characteristics of the previously known cell population. Also, the culturing of cells at a particular cell density does not make the cells *per se* different.

The Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether or not Applicants' cells differ and, if so, to what extent, from that discussed in the references including the ability of the cell population to maintain its doubling rate. Therefore, with the showing of the references, the burden of establishing

non obvious by objective evidence is shifted to Appellants. Significantly, Appellants provide no factual evidence whatsoever to refute the holding of anticipation or obviousness. Note specifically that on the current record the only way of overcoming such a clear holding of anticipation is factual proof that the rejection is in error. *See* MPEP § 2112, disclosing that once a proper holding of anticipation is made, the burden shifts to applicant to demonstrate an unobvious difference between the claims and the prior art. *See also*, *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) ("the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product").

[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on `inherency' under 35 U.S.C. 102, on `prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product - by - process claims. Quoting *In re Fitzgerald,* 619 F. 2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (itself quoting In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 - 34 (CCPA 1977)).

Note that MPEP § 706.3(e) states that:

> [w]hen the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 35 U.S.C. 102 or 35 U.S.C. 103 of the statute is appropriate. As a practical matter, the Patent and Trademark Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith. A lesser burden of proof is required to make out a case of prima facie obviousness for product-by-process claims because of their

peculiar nature than when a product is claimed in the conventional fashion. *In re Brown*, 59 CCPA 1063, 173 USPQ 685 (1972) ; *In re Fessmann*, 180 USPQ 324 (CCPA1974).

In conclusion, the cell population claimed is a cell population which is derived from bone marrow by taking an aspirate of the bone marrow and culturing it until adherent CFUs form and isolating said CFUs. The cells of Haynesworth are a cell population claimed is a cell population which is derived from bone marrow by taking an aspirate of the bone marrow and culturing it until adherent CFUs form and isolating said CFUs. Further, the cells do not differ in any disclosed function or utility. As such, the disclosed MSCs of Haynesworth anticipate the claimed invention.

(10) Response to Argument

Appellants have argued that the claimed cell population is not a population of Mesenchymal Stem Cells (MSC) because they express different cell surface markers. This argument has been fully considered but it is unclear that the presence of one or even a few differences in cell surface markers is indicative of a new cell type. This is particularly true wherein there is no apparent functional change in the cell.

Furthermore, it is apparent from the literature on the subject that not all cell surface markers are conserved. i.e. are always present or absent from a particular cell type. As such, the claimed cells would appear to be functionally the same as what the prior art calls mesenchymal stem cells differing only in the presence or absence of a few

cell surface markers that have not be shown to have any bearing on the fundamental functions or characteristics of the cells. To support his argument, in the final rejection, the examiner cited three review articles (Baksh, Lodie & Chamberlain) which all show that MSCs have some small phenotypic differences depending on their culture conditions. Appellants did not choose to dispute this argument.

Doubling rate though a property of a cell is completely dependent on the culture conditions used. Appellants' comparisons of doubling rates disclosed in the prior art with their optimized doubling culture conditions are not directly comparable and as such fail to distinguish the prior art cells from the claimed cells.

Appellants have attempted to differentiate the claimed population from MSCs by indicating that the method for preparing the population differ from the methods of preparing/isolating MSCs. An analysis of Appellants' specification does not seem to yield a description of a method which would yield cells other than MSCs.

Applicants argue that the claimed cells are isolated from a low density gradient fraction and that the claimed cells are isolated from a high density gradient fraction. However, as indicated in the declaration of Appellants, the media and methods for isolation are not the same and as such it is unclear how that cells can be established as different based on the density gradient fraction from which they are isolated. It should be noted as well that the claims are not limited to a functional definition of which fraction the cells are isolated from. Claim 97 would be suggestive that the density gradient

fraction is not critical. Appellants' arguments and the claims would appear to be in conflict.

It is unclear from Appellants' specification what is critical to the production of a cell population which is different from MSCs. Appellants' specification (cited by applicant for support of new claim 97) does not demonstrate a method which has critical steps which would yield a population other than MSCs:

> Human bone marrow cells are obtained from healthy human donors by aspirations of the iliac crest and bone marrow stromal cell populations obtained employing well established techniques. For example, substantially homogenous cell populations which co-express CD49c and CD90 are obtained from human iliac crest bone marrow aspirates and processed to mononuclear cell fractions from which bone marrow stromal cells are selectively propagated *in vitro* based upon their propensity to attach to plastic and divide in response to defined cell culture medium. The plastic-adherent cells are optimally grown at a cell concentration that encourages virtually only the self-renewing cells, referred to as colony-forming unit fibroblast-like cells (Cfu-f), to proliferate. The Cfu-f-derived cells are analyzed for cells which co-express CD49c and CD90 and sub-cultured to produce a substantially homogenous cell population which co-express CD49c and CD90.

Further Appellants argue that certain marker expression profiles distinguish the claimed invention from the prior art but the expression (or lack thereof) of these markers is neither claimed nor disclosed in the specification.

The majority of Appellants' arguments as summarized on page 27 of the brief are based on reported/alleged differences which have not been substantiated using the same culture conditions and, as any cell biologist of any skill in the art would know, cells react differently based on their culture conditions.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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